#11

Appendix 1

NPYantagonist.txt

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* * * * * * * * * * * * * * * * STN  Karlsruhe * * * * * * * * * * * * * * * *
FILE 'HOME' ENTERED AT 11:36:49 ON 20 JAN 2003

=> file caplus
COST IN EUROS                                          SINCE FILE      TOTAL
                                                          ENTRY     SESSION
FULL ESTIMATED COST                                        0,30        0,30


=> s (neuropeptide y or npy?) and antagonist? and pd<20000825
         18038 NEUROPEPTIDE
        265556 Y
          7618 NEUROPEPTIDE Y
                 (NEUROPEPTIDE(W)Y)
          5598 NPY?
        189380 ANTAGONIST?
      20519302 PD<20000825
                 (PD<20000825)
L1          993 (NEUROPEPTIDE Y OR NPY?) AND ANTAGONIST? AND PD<20000825

=> logoff
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:y

STN INTERNATIONAL LOGOFF AT 11:38:27 ON 20 JAN 2003
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Appendix 2

* * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 39	Apr 23	STN Patent Forums in Scandinavia
NEWS 38	Apr 23	Federal Research in Progress (FEDRIP) now available
NEWS 37	Apr 23	BIOSIS Gene Names now available in TOXCENTER
NEWS 36	Apr 23	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 35	Apr 23	US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS 34	Apr 09	ZDB will be removed
NEWS 33	Apr 04	BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS 32	Apr 03	PAPERCHEM no longer available on STN. Use PAPERCHEM2 instead.
NEWS 31	Apr 02	LIPINSKI/CALC added for property searching in REGISTRY
NEWS 30	Apr 02	US Provisional Priorities searched with P in CA/CAplus and USPATFULL
NEWS EXPRESS		FEB 01 CURRENT WINDOWS VERSION IS V6.0d, CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP), AND CURRENT DISCOVER FILE IS DATED 07 August 2001
NEWS HOURS		May 16, 2002 NEW STN OPERATING HOURS

* * * * * * * * * * * * * * * STN Karlsruhe * * * * * * * * * * * * * * *
FILE 'HOME' ENTERED AT 12:53:40 ON 24 MAY 2002

=> file caplus

COST IN EUROS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0,30	0,30

FILE 'CAPLUS' ENTERED AT 12:53:53 ON 24 MAY 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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FILE COVERS 1907 - 24 May 2002  VOL 136 ISS 21
FILE LAST UPDATED: 22 May 2002  (20020522/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

CAS roles have been modified effective December 16, 2001. Please
check your SDI profiles to see if they need to be revised. For
information on CAS roles, enter HELP ROLES at an arrow prompt or use
the CAS Roles thesaurus (/RL field) in this file.

=> s (neuropeptide y or npy?) and (agonist? or antagonist?) and pd<19971219
         17295 NEUROPEPTIDE
        256250 Y
          7258 NEUROPEPTIDE Y
                 (NEUROPEPTIDE(W)Y)
          5338 NPY?
        112431 AGONIST?
        180281 ANTAGONIST?
      18113004 PD<19971219
                 (PD<19971219)
L1          909 (NEUROPEPTIDE Y OR NPY?) AND (AGONIST? OR ANTAGONIST?) AND PD<19
                971219

=> s y1? or y2? or y5?
         14982 Y1?
         39781 Y2?
          1324 Y5?
L2        51155 Y1? OR Y2? OR Y5?

=> s l1 and l2
L3          302 L1 AND L2

=> display
ENTER (L3), L# OR ?:l3
ENTER ANSWER NUMBER OR RANGE (1):1-20
ENTER DISPLAY FORMAT (BIB):bib abs

L3   ANSWER 1 OF 302  CAPLUS  COPYRIGHT 2002 ACS
AN   1999:748255  CAPLUS
DN   132:716
TI   Recombinant mammalian cells and method for screening for   ***agonists***
     or   ***antagonists***   of rat and human   ***Y5***
       ***neuropeptide***      ***Y***   receptors
IN   Gerald, Christophe P. G.; Weinshank, Richard L.; Walker, Mary W.;
     Branchek, Theresa
PA   Synaptic Pharmaceutical Corporation, USA
SO   U.S., 100 pp., Cont.-in-part of U.S. Ser. No. 566,096.
     CODEN: USXXAM
DT   Patent
LA   English
FAN.CNT 4
     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
PI   US 5989920         A    19991123      US 1996-668650   19960604
     US 5602024         A    19970211      US 1994-349025   19941202 <--
     US 5968819         A    19991019      US 1995-566096   19951201
```

WO 9746250 A1 19971211 WO 1997-US9504 19970604 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
AU 9732952 A1 19980105 AU 1997-32952 19970604
EP 1007073 A1 20000614 EP 1997-928786 19970604
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
PRAI US 1994-349025 A2 19941202
US 1995-566096 A2 19951201
US 1996-668650 A2 19960604
US 1997-803600 A 19970221
WO 1997-US9504 W 19970604

AB The title recombinant cells and their use are disclosed. The cDNAs for ***Y5*** ***neuropeptide*** ***Y*** receptors of human, rat and dog were cloned and sequenced. Pharmacol. characterization of the receptors in recombinant COS-7 cells, anal. of ***Y5*** receptor effects on adenyl cyclase activity in recombinant 293 cells, and Northern blot anal. of rat tissues are presented. ***Y5*** selective compds. were synthesized and their ***antagonist*** activity at human ***Y5*** receptors were demonstrated. Some of these compds. inhibited food intake in rats.

RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 302 CAPLUS COPYRIGHT 2002 ACS
AN 1999:748233 CAPLUS
DN 132:715
TI Recombinant mammalian cells and method for identification of ***neuropeptide*** ***Y*** -binding substances
IN Gerald, Christophe; Walker, Mary W.; Branchek, Theresa; Weinshank, Richard L.
PA Synaptic Pharmaceutical Corporation, USA
SO U.S., 79 pp., Cont.-in-part of U.S. 5,545,549.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 6

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5989834	A	19991123	US 1996-687355	19961126
US 5545549	A	19960813	US 1994-192288	19940203 <--
WO 9521245	A1	19950810	WO 1995-US1469	19950203 <--

W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

PRAI US 1994-192288 A2 19940203
WO 1995-US1469 W 19950203

AB Disclosed are cells expressing rat or human ***Y2*** receptors which may be used to screen for ***agonists*** / ***antagonists*** . Thus, the cDNAs for one human and two rat ***Y2*** receptors were cloned. CHO and COS7 cells transiently expressing the human ***Y2*** receptor were used for pharmacol. characterization of this receptor. 3T3 and 293 cells expressing the receptor were used for anal. of second messenger response, i.e., inhibition of adenyl cyclase activity, and intracellular Ca2+ mobilization.

RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 302 CAPLUS COPYRIGHT 2002 ACS
AN 1999:670094 CAPLUS
DN 131:307682
TI DNA encoding a hypothalamic atypical ***neuropeptide*** ***Y*** /peptide YY receptor (***Y5***)
IN Gerald, Christophe P. G.; Weinshank, Richard L.; Walker, Mary W.; Branchek, Theresa
PA Synaptic Pharmaceutical Corporation, USA
SO U.S., 87 pp., Cont.-in-part of U.S. 5,602,024.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	US 5968819	A	19991019	US 1995-566096	19951201	
	US 5602024	A	19970211	US 1994-349025	19941202	<--
	CA 2174529	AA	19960603	CA 1995-2174529	19951201	<--
	US 5989920	A	19991123	US 1996-668650	19960604	
	US 6316203	B1	20011113	US 1998-200673	19981125	
PRAI	US 1994-349025	A2	19941202			
	US 1995-566096	A2	19951201			

GI

/ Structure 1 in file .gra /

AB This invention provides methods of modifying feeding behavior, including increasing or decreasing food consumption, e.g., in connection with treating obesity, bulimia or anorexia. These methods involve administration of compds. are selective ***agonists*** or ***antagonists*** or the ***Y5*** receptor. One such compd. has the structure: I. In addn., this invention provides an isolated nucleic acid mol. encoding a ***Y5*** receptor, an isolated ***Y5*** receptor protein, vectors comprising an isolated nucleic acid mol. encoding a ***Y5*** receptor, cells comprising such vectors, antibodies directed to the ***Y5*** receptor, nucleic acid probes useful for detecting nucleic acid encoding ***Y5*** receptors, antisense oligonucleotid s complementary to any unique sequences of a nucleic acid mol. which ncodes a ***Y5*** receptor, and nonhuman transgenic animals which express DNA a normal or a mutant ***Y5*** receptor.

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 302 CAPLUS COPYRIGHT 2002 ACS
AN 1999:289424 CAPLUS
DN 130:311819
TI Preparation of arylpyrazines and analogs as neuropeptide ***Y1*** receptor ***antagonists***
IN Peterson, John Matthew; Blum, Charles Albert; Cai, Guolin; Hutchison, Alan Jeffrey
PA Pfizer Inc., USA
SO U.S., 8 pp., Cont.-in-part of U.S. Ser. No. 478,383, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5900415	A	19990504	US 1997-817641	19970429
	WO 9614307	A2	19960517	WO 1995-US14472	19951107 <--

W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

	CN 1205005	A	19990113	CN 1995-196081	19951107
PRAI	US 1995-478383	B2	19950607		
	US 1995-484974	B2	19950607		
	WO 1995-US14472	W	19951107		
	US 1994-335475	A2	19941107		
	US 1995-474383	A2	19950607		

OS MARPAT 130:311819
GI

/ Structure 2 in file .gra /

AB Title compds. [I; R = (un)substituted Ph; R1,R2 = H or alkyl; R3,R4 = H, alkyl, alkoxy; R7 = Ph, pyridyl, thienyl, etc.; Z1 = O, S, NR5, CR5R6; R5 = alkyl, Ph, pyridyl, etc.; R6 = H, OH, NH2, alkyl, alkoxy, etc.; Z2 = (CH2)1-3; Z3 = (CH2)2-4] were prepd. Thus, 1-phenylpiperazine was condensed with cyclohexanone and KCN and the product treated with PhMgBr to give 1-phenyl-4-(1-phenylcyclohexyl)piperazine. Data for biol. activity of I were given.
RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 302 CAPLUS COPYRIGHT 2002 ACS
AN 1998:640182 CAPLUS
DN 130:33081
TI Peptide YY and ***neuropeptide*** ***Y*** : reciprocal control of digestion via modulation of the brain-gut axis
AU Rogers, Richard C.; Hermann, Gerlinda E.
CS Department of Physiology, Ohio State University, Columbus, OH, 43210-1218,

USA
SO Biomedical Reviews (***1997***), 8, 55-69
CODEN: BMREES; ISSN: 1310-392X
PB Bulgarian-American Center
DT Journal; General Review
LA English
AB A review, with 60 refs. Peptide tyrosine-tyrosine (PYY) and neuropeptide tyrosine (***NPY***) are emerging as potent central nervous system regulators of digestive functions. There is, however, considerable debate concerning the mechanisms and even the direction of autonomic effects mediated by these peptides. PYY is thought to be the hormonal "enterogastrone" released by the ileum after feeding. This peptide acts on vagal reflex control circuits in the dorsal vagal complex (DVC) of the medulla oblongata to reduce gastric motility, i.e. the "ileal brake". However, equally convincing evidence is available to suggest that PYY and its close structural relative ***NPY*** may also act in the DVC to increase gastric motility through vagal mechanisms. This activation effect, particularly of ***NPY*** , has been linked to the increase in digestive functions seen at the onset of feeding behavior, i.e. Pavlov's "cephalic phase". We hypothesize that the confounding observations produced by these peptides are due to ***agonist*** effects on two different receptor types referred to as ***Y1*** and ***Y2*** . Both receptors are present in the DVC but may be accessed differentially by peripheral humoral (PYY) vs. central neurotransmitter (***NPY***) pathways. Our expts. show that the hormonal effect of PYY to suppress gastric functions such as the "ileal brake" is consistent with the activation of the ***Y2*** receptor in the DVC, while ***NPY*** -ergic effects to increase gastric functions are mediated by the ***Y1*** receptor. These results are corroborated by neurophysiol. studies of the effects of ***Y1*** and ***Y2*** ***agonist*** peptides on single vagal efferent neurons. The seemingly paradoxical effects of PYY and ***NPY*** on the central neural control of gastric motility are reviewed in terms of the possible differential localization of ***Y1*** vs. ***Y2*** receptors within the DVC. Specific ref. is also made to recent observations that PYY is rapidly converted to a ***Y2*** ***agonist*** by an ubiquitous dipeptidyl aminopeptidase.
RE.CNT 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 302 CAPLUS COPYRIGHT 2002 ACS
AN 1998:159325 CAPLUS
DN 128:266087
TI ***Neuropeptide*** ***Y*** ***Y1*** receptor ***antagonist*** (BIBP 3226) attenuates stress evoked tachycardia in conscious spontaneously hypertensive rats
AU Zhang, Weiguo; Lundberg, Jan M.; Thoren, Peter
CS Department of Physiology and Pharmacology, Karolinska Institute, Stockholm, 171 77, Swed.
SO Cardiovasc. Drugs Ther. (***1997***), 11(6), 801-806
CODEN: CDTHET; ISSN: 0920-3206
PB Kluwer Academic Publishers
DT Journal
LA English
AB The effects of a novel ***neuropeptide*** ***Y*** (***NPY***) ***Y1*** receptor ***antagonist*** on resting mean blood pressure (MBP) and heart rate (HR) were obsd. in conscious spontaneously hypertensive rats (SHR). The interference of the ***antagonist***

with cardiovascular responses to mental stress and administration of exogenous ***NPY*** were also investigated. SHR randomly received either the ***NPY*** ***Y1*** receptor ***antagonist*** (BIBP 3226) or its inactive enantiomer (BIBP 3435) as an infusion (6 mg/kg/h for 1.5 h). Before, during, and after the infusion, rats were first stressed with a jet of air and then given a bolus injection of exogenous ***NPY*** (2 nmol/kg). There was no statistically significant difference of resting MBP and HR between the ***antagonist*** and enantiomer groups before, during, or after infusion. The stress-induced max. increase in HR was significantly reduced during ***antagonist*** infusion. The effects of exogenous ***NPY*** on both MBP and HR were significantly attenuated by ***antagonist*** infusion (resp.), and the effect lasted at least 1 h after the end of the infusion. Plasma catecholamine levels in response to stress were not significantly different between the two groups. The results suggest that endogenous ***NPY*** ***Y1*** -receptor mechanisms may be of minor importance in short-term regulation of MBP and HR in conscious adult SHR, but may be involved in the response to mental stress.

L3 ANSWER 7 OF 302 CAPLUS COPYRIGHT 2002 ACS
AN 1998:60164 CAPLUS
DN 128:163216
TI ***Neuropeptide*** ***Y*** ***Y1*** receptor blockade does not alter adrenergic nerve responses of the rat tail artery
AU Duckles, Sue P.; Adner, Mikael; Edvinsson, Lars; Krause, Diana N.
CS Coll. Med., Univ. California, Irvine, CA, 92697, USA
SO Eur. J. Pharmacol. (***1997***), 340(1), 75-79
CODEN: EJPHAZ; ISSN: 0014-2999
PB Elsevier Science B.V.
DT Journal
LA English
AB Using the selective ***neuropeptide*** ***Y*** ***Y1*** receptor ***antagonist*** , BIBP3226 [N2-(diphenylacetyl)-N-[(4-hydroxyphenyl)methyl]-D-argininamide], the role of endogenous ***neuropeptide*** ***Y*** in mediating vasoconstrictor responses to adrenergic nerve stimulation was investigated by recording isometric force from isolated rat tail artery segments. BIBP3226 had no effect on contractile responses to adrenergic nerve stimulation (10 pulses; 0.5-2 Hz), but it completely blocked the enhancement of contraction produced by exogenous ***neuropeptide*** ***Y*** . When frequency and train length of the transmural nerve stimulation were increased (100 pulses; 1-16 Hz), contractile responses were still unaffected by BIBP3226. A peptidase inhibitor mixt. known to increase responses to exogenous ***neuropeptide*** ***Y*** was added; however, BIBP3226 still did not influence contractile responses to adrenergic nerve stimulation. Thus, contractile responses to adrenergic nerve stimulation in the rat tail artery do not appear to involve the release and postjunctional action of endogenous ***neuropeptide*** ***Y*** ; however, exogenous ***neuropeptide*** ***Y*** does potentiate these responses by acting on ***Y1*** receptors.

L3 ANSWER 8 OF 302 CAPLUS COPYRIGHT 2002 ACS
AN 1998:20382 CAPLUS
DN 128:149836

TI Sympathetic and parasympathetic interaction in vascular and secretory control of the nasal mucosa in anesthetized dogs
AU Revington, Maureen; Lacroix, J. Silvain; Potter, Erica K.
CS Prince of Wales Medical Research Institute, Prince of Wales Hospital, Sydney, NSW 2031, Australia
SO J. Physiol. (Cambridge, U. K.) (***1997***), 505(3), 823-831
CODEN: JPHYA7; ISSN: 0022-3751
PB Cambridge University Press
DT Journal
LA English
AB In dogs anesthetized with pentobarbitone, elec. stimulation of the parasympathetic nerve fibers to the nasal mucosa evoked frequency dependent increases in both nasal arterial blood flow and nasal secretion. Blood flow was measured using a transonic flow probe placed around the artery. Sympathetic nerve stimulation for 3 min at 10 Hz evoked significant and prolonged (>30 min) attenuation of the vasodilator and secretory responses to subsequent parasympathetic stimulation. I.v. and intranasal administration of the ***neuropeptide*** ***Y*** (***NPY***) analog N-acetyl [Leu28,Leu31] ***NPY*** 24-36, a selective ***NPY*** ***Y2*** receptor ***agonist*** (20 nmol kg-1), significantly attenuated both vasodilator and secretory effects of subsequent parasympathetic nerve stimulation. When given i.v., the inhibitory effect of this ***Y2*** receptor ***agonist*** on vascular and secretory effects of parasympathetic nerve stimulation was rapid in onset (5 min) and lasted for more than 60 min. The modulatory effect of the ***Y2*** receptor ***agonist*** was also seen with intranasal administration, but was slower in onset (15 min), and lasted less than 45 min. The effects of the intranasal pretreatment with the ***Y2*** receptor ***agonist*** were significantly prolonged in the presence of the endopeptidase inhibitor phosphoramidon (10 nM). Atropine pretreatment did not significantly reduce the change in vascular conductance evoked by parasympathetic nerve stimulation. Subsequent pretreatment with the ***NPY*** ***Y2*** receptor ***agonist*** N-acetyl [Leu28,Leu31] ***NPY*** 24-36 reduced the stimulation induced increase in conductance by 30%. Nasal secretion was reduced by 70% following pretreatment with atropine and a further 30% by pretreatment with the ***NPY*** ***Y2*** receptor ***agonist*** . Dose dependent vasodilator and secretory effects of local intra-arterial infusion of acetylcholine and vasoactive intestinal peptide were not modified by the ***NPY*** ***Y2*** ***agonist*** . Total protein and albumin concn. were measured in nasal lavage fluid collected after nerve stimulation. Atropine pretreatment increased the percentage of the total protein that was albumin in nasal lavage fluid. Neither sympathetic nerve stimulation nor ***Y2*** receptor ***agonist*** pretreatment further modified the albumin exudation (a marker of vascular permeability) in nasal fluid lavage collected after parasympathetic nerve stimulation. The authors propose that sympathetic nerve stimulation releases ***NPY*** , which acts on ***Y2*** receptors, probably located on parasympathetic nerve endings, to attenuate both vasodilatation and nasal secretion evoked by subsequent parasympathetic nerve stimulation. This effect is also obsd. after pretreatment with the ***Y2*** -selective ***NPY*** analog N-acetyl [Leu28,Leu31] ***NPY*** 24-36.

L3 ANSWER 9 OF 302 CAPLUS COPYRIGHT 2002 ACS
AN 1998:1498 CAPLUS
DN 128:61807

TI Preparation of alanine-containing analogs of ***NPY*** (24-36) as ***neuropeptide*** ***Y*** receptor ***agonists***

IN Potter, Erica

PA Peptech Limited, Australia; CRC for Biopharmaceutical Research Limited; Potter, Erica

SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9746579	A1	19971211	WO 1997-AU352	19970605 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9729449	A1	19980105	AU 1997-29449	19970605
	EP 907658	A1	19990414	EP 1997-923672	19970605
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2001508025	T2	20010619	JP 1998-500017	19970605
	CN 1322212	A	20011114	CN 1997-197106	19970605
PRAI	AU 1996-290	A	19960605		
	WO 1997-AU352	W	19970605		

OS MARPAT 128:61807

AB Title compds. X1X2X3X4X5X6X7X8X9X10X11X12X13X14X15 [X1 = H, acyl, amino acid; X2 = Leu, Ile, Val, Nle, Sar, Gly, Ala, Aib, D-Leu, D-Ile, D-Val, D-Ala, D-Nle; X3 = Arg, Lys, Orn, Ala, Dbu, His; X4 = His, Lys, Arg, Ala, Gly, Ser, Thr, Asn, Gln, Aib; X5 = Tyr, Phe, Ala, Gly, Ser, Thr, Asn, Gln, Aib; X6 = Leu, Ile, Val, Ala, Arg, Nle; X7 = Asn, Ala, Gln; X8, X9 = Leu, Ile, Val, Ala, Aib, Nle; X10 = Thr, Ala, Ser; X11 = Arg, Lys, Orn; X12 = Gln, Pro, Asn; X13 = Arg, Lys, Orn; X14 = Tyr, Phe, His, Trp, D-Tyr, D-Phe, D-His, D-Trp; X15 = OH, NH2, (substituted) amino, amino acid amide, etc.; wherein at least one of X2-10 is Ala] were prepd. as ***neuropeptide*** ***Y*** (***NPY***) receptor ligands derived from the ***NPY24*** -36 amino acid sequence. The peptides were prepd. by std. Boc or Fmoc solid-phase chem., and they may be used in the treatment of rhinitis, respiratory diseases and vasoconstriction predisposing to acute renal failure. In an ***Y2*** receptor binding assay, for example, Ac[Leu28,Ala31] ***NPY*** (24-36) had an IC50 value of 0.06 nM compared with 0.5 nM of AcNPY(24-36).

L3 ANSWER 10 OF 302 CAPLUS COPYRIGHT 2002 ACS

AN 1997:812197 CAPLUS

DN 128:98586

TI Methods of modifying feeding behavior, compounds useful in such methods, and DNA encoding a hypothalamic atypical ***neuropeptide*** ***Y*** /peptide YY receptor

IN Gerald, Christophe P. G.; Weinshank, Richard L.; Walker, Mary W.; Branchek, Theresa

PA Synaptic Pharmaceutical Corporation, USA; Gerald, Christophe P. G.; Weinshank, Richard L.; Walker, Mary W.; Branchek, Theresa

SO PCT Int. Appl., 272 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9746250	A1	19971211	WO 1997-US9504	19970604 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5989920	A	19991123	US 1996-668650	19960604
AU 9732952	A1	19980105	AU 1997-32952	19970604
EP 1007073	A1	20000614	EP 1997-928786	19970604
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PRAI US 1996-668650	A2	19960604		
US 1997-803600	A	19970221		
US 1994-349025	A2	19941202		
US 1995-566096	A2	19951201		
WO 1997-US9504	W	19970604		

AB The invention provides methods of modifying feeding behavior, including increasing or decreasing food consumption, e.g., in connection with treating obesity, bulimia or anorexia. These methods involve administration of compds. that are selective ***agonists*** or ***antagonists*** for the ***Y5*** receptor. In addn., this invention provides an isolated nucleic acid mol. encoding a ***Y5*** receptor, an isolated ***Y5*** receptor protein, vectors comprising an isolated nucleic acid mol. encoding a ***Y5*** receptor, cells comprising such vectors, antibodies directed to the ***Y5*** receptor, nucleic acid probes useful for detecting nucleic acid encoding ***Y5*** receptors, antisense oligonucleotides complementary to any unique sequences of a nucleic acid mol. which encodes a ***Y5*** receptor, and nonhuman transgenic animals which express DNA encoding a normal or a mutant ***Y5*** receptor. Expression cloning isolated a novel Y-type receptor from a rat hypothalamic cDNA library, along with its pharmacol. characterization, in situ localization, and human and canine analogs. This newly cloned receptor subtype, referred to as the ***Y5*** subtype, is linked to the "atypical ***Y1*** " feeding response. ***Neuropeptide*** ***Y*** -related peptides bound to and activated the ***Y5*** receptor such a rank order of potency identical to that described for the feeding response, and the ***Y5*** receptor was neg. coupled to cAMP accumulation. Thus, various synthetic, nonpeptidyl compds. which bind to the ***Y5*** receptor and act as ***antagonists*** , may alter the subject's consumption of food and thereby modify the subject's feeding behavior.

L3 ANSWER 11 OF 302 CAPLUS COPYRIGHT 2002 ACS
AN 1997:803256 CAPLUS
DN 128:98124
TI ***Neuropeptide*** ***Y*** (***NPY***) and peptide YY (PYY) effects in the epididymis of the guinea pig: evidence of a pre-junctional

PYY-selective receptor
AU Haynes, John M.; Hill, Stephen J.; Selbie, Lisa A.
CS Dep. Physiol. Pharmacol., Med. Sch. Queen's Med. Cent., Nottingham, NG7 2 UH, UK
SO Br. J. Pharmacol. (***1997***), 122(7), 1530-1536
CODEN: BJPCBM; ISSN: 0007-1188
PB Stockton Press
DT Journal
LA English
AB The effects of peptide YY (PYY), ***neuropeptide*** ***Y*** (***NPY***) and structurally related peptides upon field stimulation-induced and phenylephrine-mediated contractile responses in the cauda epididymis of the guinea pig were investigated. Prepns. of cauda epididymis responded to field stimulation with contractions which were completely attenuated by both the neurotoxin, tetrodotoxin (500 nM), and also the .alpha.-adrenoceptor ***antagonist*** , phentolamine (3 .mu.M). PYY and the truncated peptide analog PYY(3-36) inhibited field stimulation-induced contractions (pIC50: 8.9 and 9.4, resp.). Pancreatic polypeptide (PP, up to 1 .mu.M), ***NPY*** (up to 100 nM) and the ***NPY*** analogs [Leu31,Pro34] ***NPY*** and ***NPY*** (13-36) (both up to 1 .mu.M) had no significant effect. The ***NPY*** Y, receptor ***antagonist*** BIBP 3226 at 750 nM and 7.5 .mu.M did not affect the PYY-mediated inhibition of field stimulation-induced contractions (pIC50 8.9 and 9.0, resp.). In the presence of BIBP 3226 (7.5 .mu.M), ***NPY*** inhibited field stimulation-induced contractions (pIC50 8.0). ***NPY*** , PYY and PYY(3-36) inhibited [3H]-noradrenaline release from prepns. of epididymis (pIC50 values 7.9, 9.6 and 10.0, resp.). The ***agonists*** PP and [Leu31,Pro34]PYY (both up to 100 nM) were without significant effect. In prepns. of cauda epididymis, stimulated with threshold concns. of the .alpha.1-adrenoceptor ***agonist*** , phenylephrine (1 .mu.M), both ***NPY*** and PYY elicited concn.-dependent increases in contractile force (with pEC50 values of 8.9 and 8.6, resp.). The effects of both ***NPY*** and PYY were antagonized by preincubation with BIBP 3226 (75 nM: apparent pKB 8.3 and 8.2, resp.). The peptide analogs ***NPY*** (13-36), PYY(3-36) and [Leu31,Pro34] ***NPY*** did not significantly augment responses to threshold concns. of phenylephrine. These results are consistent with the proposal that distinct ***NPY*** receptors mediate the (prejunctional) inhibition of field stimulation-induced contractions and the (postjunctional) potentiation of responses to phenylephrine in the cauda epididymis of the guinea pig. The rank order of ***agonist*** potency (***NPY*** .gtoreq. PYY >> ***NPY*** (13-36), [Leu31,Pro34] ***NPY*** and PYY(3-36)) and the high potency of BIBP 3226 indicate that the postjunctional receptor may be ***Y1*** -like. The rank orders of ***agonist*** potency in inhibiting field stimulation-induced contractile responses and [3H]-noradrenaline release (PYY(3-36) .gtoreq. PYY > ***NPY*** >> PP, ***NPY*** (13-36). [Leu31,Pro34] ***NPY*** and PYY(3-36) .gtoreq. PYY > ***NPY*** >> PP, [Leu31,Pro34]PYY, resp.) are consistent with the action of these peptides at a PYY-preferring receptor subtype, which may be distinct from the presently characterized ***NPY*** receptor subtypes.

L3 ANSWER 12 OF 302 CAPLUS COPYRIGHT 2002 ACS
AN 1997:795605 CAPLUS
DN 128:98089
TI Distribution of [Leu31,Pro34] ***NPY*** -sensitive, BIBP3226-insensitive

[125I]PYY(3-36) binding sites in rat brain: possible relationship to ***Y5*** ***NPY*** receptors

AU Widdowson, P. S.; Buckingham, R.; Williams, G.

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SO Brain Res. (***1997***), 778(1), 242-250
CODEN: BRREAP; ISSN: 0006-8993

PB Elsevier Science B.V.

DT Journal

LA English

AB Recently, using mol. cloning approaches, three new ***neuropeptide*** ***Y*** (***NPY***)/peptide YY (PYY) receptors have been described in rodent brain, with pharmacol. profiles that differ from the three previously described ***Y1*** , ***Y2*** and Y3 ***NPY*** receptors and the Y4 pancreatic polypeptide- (PP-) preferring receptor. Two of these new receptors are spice variants and are called ***Y5*** receptors, while a third receptor has been called Y6 and has been suggested to be expressed only in the mouse. In the absence of a totally selective ***Y5*** and/or Y6 radioligands, the authors have examd. [125I]PYY(3-36) binding, which binds ***Y2*** and ***Y5*** /Y6 receptors, using homogenate assays and quant. receptor autoradiog. to study the distribution of the three newly discovered ***Y5*** /Y6 receptors by masking binding to ***Y1*** receptors with high concns. of the non-peptidergic selective ***Y1*** ***antagonist*** , BIBP3226, and using either [Leu31,Pro34] ***NPY*** or human PP to mask binding to ***Y5*** and Y6 receptors, leaving binding to ***Y2*** receptors. Using this approach, [125I]PYY(3-36) labels a small population of ***Y1*** receptors and a larger population of binding sites that are insensitive to BIBP3226, human PP and [Leu31,Pro34] ***NPY*** , presumed to be ***Y2*** receptors. There was also [125I]PYY(3-36) binding to sites sensitive to ***NPY*** , human PP and [Leu31,Pro34] ***NPY*** , but insensitive to BIBP3226, located in the hypothalamus, amygdala, hippocampus and thalamus. As one of the recently cloned

Y5 receptors is synthesized in these regions, as shown by in-situ hybridization techniques, the authors suggest that the small population of [125I]PYY(3-36) binding sites which are sensitive to human PP and [Leu31,Pro34] ***NPY*** , but insensitive to BIBP3226, may represent binding to ***Y5*** receptors. The authors have been unable, however, to visualize a smaller population of Y6 receptors which are labeled by [125I]PYY3-36 and sensitive to [Leu31,Pro34] ***NPY*** , but not to BIBP3226 and human PP, confirming that the murine Y6 receptor does not appear to be expressed in rat brain.

L3 ANSWER 13 OF 302 CAPLUS COPYRIGHT 2002 ACS

AN 1997:795442 CAPLUS

DN 128:97224

TI ***Neuropeptide*** ***Y*** receptor ***antagonists*** in obesity

AU Gehlert, Donald R.; Hipskind, Philip A.

CS USA

SO Expert Opin. Invest. Drugs (***1997***), 6(12), 1827-1838
CODEN: EOIDER; ISSN: 0967-8298

PB Ashley Publications

DT Journal; General Review

LA English

AB A review, with 104 refs. ***Neuropeptide*** ***Y*** (***NPY***

) is a 36 amino acid amidated peptide with high sequence homol. to the endocrine peptides, peptide YY (PYY) and pancreatic polypeptide (PP). These peptides appear to interact with a family of receptors that possess high affinity for one or more of these peptides. Five members of the receptor family have been cloned, with several addnl. members postulated through pharmacol. evidence. All are members of the seven transmembrane domain G-protein coupled receptor family. The ***Y1*** receptor is the best characterized, with several nonpeptide ***antagonists*** available. This receptor appears to mediate a constriction of the peripheral vasculature and the "anxiolytic" effects of centrally administered ***NPY*** . Less is known about the other receptors in the family. The ***Y2*** receptor is believed to be presynaptic and mediates a redn. in neurotransmitter release. The Y4 receptor seems to be the receptor for PP, with high amts. of mRNA for this receptor found in the periphery, but lower levels in the brain. The ***Y5*** receptor is expressed in the hypothalamus and has been postulated to be the receptor that mediates the increased food consumption seen following centrally administered ***NPY*** . Finally, the Y6 receptor has been cloned in the mouse and other species, but does not appear to encode a functional gene product in humans. Several types of nonpeptide ***Y1*** and a series of ***Y5*** ***antagonists*** have been described in the patent literature, though these compds. have limitations that will confine their use to preclin. studies. Nevertheless, considerable progress has been made in understanding the role of ***NPY*** and its receptors in exptl. obesity. The next step will be the discovery of potent and selective nonpeptide ***antagonists*** , to add further credence to the therapeutic potential.

L3 ANSWER 14 OF 302 CAPLUS COPYRIGHT 2002 ACS
AN 1997:792562 CAPLUS
DN 128:60194
TI Marked decrease of ***neuropeptide*** ***Y*** ***Y2*** receptor binding sites in the hippocampus in murine prion disease
AU Diez, Margarita; Koistinaho, Jari; Dearmond, Stephen J.; Groth, Darlene; Prusiner, Stanley B.; Hokfelt, Tomas

CS Department of Neuroscience, Karolinska Institutet, Stockholm, S-171 77, Swed.
SO Proceedings of the National Academy of Sciences of the United States of America (***1997***), 94(24), 13267-13272
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
AB Using autoradiog. binding methodol. with monoiodinated peptide YY together with the ***agonists*** ***neuropeptide*** ***Y*** (***NPY***) and ***NPY*** (13-36), as well as in situ hybridization with oligonucleotide probes complementary to the ***NPY*** ***Y2*** receptor (***Y2*** -R) mRNA, we have studied whether or not intracerebral prion inoculation affects ***Y2*** -Rs in male CD-1 mice. Monoiodinated peptide YY binding, mainly representing ***Y2*** -Rs, was down-regulated by 85% in the CA1 strata oriens and radiatum and by 50-65% in the CA3 stratum oriens 110-140 days postinoculation. In the CA3 stratum radiatum, where the mossy fibers from the dentate granul cells project, there was a significant decrease in PYY binding at 110-120 days. ***Y2*** -R mRNA, moderately expressed both in the CA1 and CA3 pyramidal cell layers and the granule cell layer in the dentate gyrus, showed a

slight, but not significant, decrease in CA3 neurons 130 days postinoculation. The results indicate that the accumulation of the scrapie prion protein in the CA1-3 region strongly inhibits ***NPY*** binding at the ***Y2*** -Rs, which, however, is only marginally due to reduced ***Y2*** -R mRNA expression. The loss of the ability of ***NPY*** to bind to inhibitory ***Y2*** -Rs may cause dysfunction of hippocampal circuits and may contribute to the clin. symptoms in mouse scrapie.

L3 ANSWER 15 OF 302 CAPLUS COPYRIGHT 2002 ACS
AN 1997:769391 CAPLUS
DN 128:44251
TI Synthesis and ***neuropeptide*** ***Y*** ***Y1*** receptor ***antagonistic*** activity of N,N-disubstituted .omega.-guanidino- and .omega.-aminoalkanoic acid amides
AU Mueller, Manfred; Knieps, Sebastian; Gessele, Karin; Dove, Stefan; Bernhardt, Guenther; Buschauer, Armin
CS Institute Pharmacy, University Regensburg, Regensburg, D-93040, Germany
SO Archiv der Pharmazie (Weinheim, Germany) (***1997***), 330(11), 333-342
CODEN: ARPMAS; ISSN: 0365-6233
PB Wiley-VCH Verlag GmbH
DT Journal
LA English

AB Potent arpromidine-type histamine H2 receptor ***agonists*** such as BU-E-76 (He 90481) were among the 1st non-peptides reported to display weak ***neuropeptide*** ***Y*** (***NPY***) ***Y1*** receptor ***antagonist*** activity. In search of new chem. leads for the development of more potent ***NPY*** ***antagonists*** , a series of N,N-disubstituted .omega.-guanidino and .omega.-aminoalkanoic acid amides were synthesized on the basis of structure-activity relationships and mol. modeling studies of arpromidine and related imidazolylpropylguanidines. In 1 group of compds. the imidazole ring was retained whereas in the 2nd group it was replaced with a phenol group representing a putative mimic of Tyr36 in ***NPY*** . Although the substitution patterns were not yet optimized, the title compds. are ***NPY*** ***Y1*** ***antagonists*** in human erythroleukemia (HEL) cells (Ca2+ assay) achieving pKB values of 6.3-6.6. For representative new substances tested in the isolated guinea pig right atrium histamine H2 receptor agonism could not be found. In the N-(diphenylalkyl)amide series, compds. with a trimethylene chain were more active ***Y1*** ***antagonists*** than the ethylene homologs. Concerning the spacer in the .omega.-amino or .omega.-guanidinoalkanoyl portion, the best activity was found in compds. with a 4- or 5-membered alkyl chain or a 1,4-cyclohexylene group. In contrast to the phenol series, in the imidazole series the compds. with a side chain amino group was considerably more potent than the corresponding strongly basic guanidines. Thus, the structure-activity relationships appear to be different for the diphenylalkylamide ***NPY*** ***antagonists*** with 1 or 2 basic groups.

L3 ANSWER 16 OF 302 CAPLUS COPYRIGHT 2002 ACS
AN 1997:759374 CAPLUS
DN 128:176473
TI Increased receptor sensitivity to ***neuropeptide*** ***Y*** in

the hypothalamus may underlie transient hyperphagia and body weight gain
AU Kalra, Pushpa S.; Dube, Michael G.; Xu, Bin; Kalra, Satya P.
CS P.O. Box, Department of Physiology, University of Florida College of Medicine, Gainesville, FL 32610-0274, 100274 JHMHC, USA
SO Regul. Pept. (***1997***), 72(2,3), 121-130
CODEN: REPPDY; ISSN: 0167-0115
PB Elsevier Science B.V.
DT Journal
LA English
AB Disruption of neural signaling by microinjection of a neurotoxin, colchicine (COL), in the ventromedial hypothalamus (VMH) of rats results in rapid and transient hyperphagia and body wt. gain. Since ***neuropeptide*** ***Y*** (***NPY***) is a potent hypothalamic orexigenic signal and continuous ***NPY*** receptor activation by intracerebroventricular (icv) ***NPY*** infusion results in hyperphagia and obesity, the authors tested the hypothesis that altered ***NPYergic*** signaling may underlie the transient hyperphagia in COL-injected rats. Immediately following COL (4 .mu.g) microinjections in the ventromedial nucleus (VMN) rats displayed hyperphagia both during the lights-on and lights-off periods. Concomitant with hyperphagia, preproNPY mRNA levels in the arcuate nucleus and ***NPY*** levels in the paraventricular nucleus decreased in a time-dependent manner. However, food intake in response to intracerebroventricular injections of ***NPY*** (29, 117 and 470 pmole) was significantly higher in COL-injected rats and the latency to initiation of feeding was markedly reduced as compared to controls. The smallest dose of ***NPY*** which was virtually ineffective in control rats, evoked near maximal intake in COL-injected rats. This enhanced response lasted for only 4 days paralleling the transient hyperphagia. The ***NPY*** ***Y1*** receptor ***antagonist*** 1229U91 (5 or 30 .mu.g/rat, icv) significantly suppressed feeding in COL-treated rats thereby indicating that hyperphagia in these rats was dependent upon endogenous ***NPY*** . Overall, these studies demonstrate that not only high levels, but low levels of ***NPY*** may also result in hyperphagia and increased body wt. and this hyperphagia may be attributed to the rapid development of ***NPY*** ***Y1*** receptor hypersensitivity.

L3 ANSWER 17 OF 302 CAPLUS COPYRIGHT 2002 ACS
AN 1997:759372 CAPLUS
DN 128:176472
TI Pharmacological characterization and selectivity of the ***NPY*** ***antagonist*** GR231118 (1229U91) for different ***NPY*** receptors
AU Matthews, Jessica E.; Jansen, Marilyn; Lyerly, Donald; Cox, Richard; Chen, Wen-Ji; Koller, Kerry J.; Daniels, Alejandro J.
CS PO Box, Department of Metabolic Diseases, Glaxo Wellcome Inc., Research Triangle Park, NC 27709-3398, 13398, USA
SO Regul. Pept. (***1997***), 72(2,3), 113-119
CODEN: REPPDY; ISSN: 0167-0115
PB Elsevier Science B.V.
DT Journal
LA English
AB ***Neuropeptide*** ***Y*** (***NPY***) is widely distributed throughout the central and peripheral nervous system and exerts a wide range of physiol. responses by activating specific receptors. In this study the authors have characterized the potency of the high affinity peptide dimer ***antagonist*** , GR231118, to displace radiolabeled

NPY /PYY from different tissues and cell lines expressing ***Y1*** or ***Y2*** receptors and from CHO cells stably transfected with human cDNA encoding for ***Y1*** , ***Y2*** and Y4 receptors. GR231118 displays high affinity for ***Y1*** and Y4 receptors, equal or better than that of ***NPY*** itself, while its activity is several fold weaker for ***Y2*** receptors. Displacement of radiolabeled PYY from rat hypothalamic membranes by GR231118, reveals the existence of high and low affinity binding sites which may be equated to ***Y1*** and ***Y2*** receptors resp. suggesting that the compd. maybe used as a tool to dissect central ***NPY*** receptors.

L3 ANSWER 18 OF 302 CAPLUS COPYRIGHT 2002 ACS
AN 1997:758822 CAPLUS
DN 128:46804
TI Time-dependent effects of ischemia on ***neuropeptide*** ***Y*** mechanisms in pig renal vascular control in vivo
AU Malmstrom, R. E.; Lundberg, J. M.
CS Division of Pharmacology, Department of Physiology and Pharmacology, Karolinska Institute, Stockholm, S-17177, Swed.
SO Acta Physiologica Scandinavica (***1997***), 161(3), 327-338
CODEN: APSCAX; ISSN: 0001-6772
PB Blackwell Science Ltd.
DT Journal
LA English
AB We have investigated the effects of ischemia on ***neuropeptide*** ***Y*** (***NPY***) mechanisms involved in sympathetic vascular control of the pig kidney in vivo. Reperfusion after 2 h of renal ischemia was assocd. with local overflow of noradrenaline (NA) but not of ***NPY*** -like immunoreactivity (-LI). Renal sympathetic nerve stimulation 10 min into reperfusion evoked markedly reduced vasoconstrictor effects and significantly less overflow of NA (reduced by 70% from the pre-ischemic conditions), whereas ***NPY*** -LI overflow was unaltered. Renal vasoconstrictor responses to exogenous peptide YY (PYY), phenylephrine and angiotensin II were strongly attenuated after this ischemic period, while vasoconstriction to .alpha.,.beta.-methylene ATP was maintained to a larger extent. The renal vascular responses and NA overflow had become partially normalized within a 2 h recovery period. In contrast, the renal vasoconstrictor response and the overflow of ***NPY*** -LI upon sympathetic nerve stimulation were enhanced after 15 min of renal ischemia. In parallel, the PYY-evoked renal vasoconstriction was selectively and markedly prolonged after the 15 min of ischemia. In the presence of the ***NPY*** ***Y1*** receptor ***antagonist*** BIBP 3226, the augmented vascular response to nerve stimulation was significantly attenuated. We conclude that reperfusion after 2 h of renal ischemia is assocd. with local overflow of NA, whereas the sympathetic nerve-evoked release of NA and the reactivity of the renal vasculature to vasoconstrictor stimuli are reversibly reduced. Furthermore, possibly due to an impaired local degrdn., the role of neurogenically released ***NPY*** in renal sympathetic vasoconstriction is enhanced after short-term (15 min) ischemia compared with control conditions.

L3 ANSWER 19 OF 302 CAPLUS COPYRIGHT 2002 ACS
AN 1997:753969 CAPLUS
DN 128:98077
TI ***Neuropeptide*** ***Y*** as a stimulator of Na+-dependent Ca2+

efflux from freshly isolated adult rat cardiomyocytes
AU Horike, Kazuya; Yoshizumi, M.; Kitagawa, Tetsuya; Itoh, Kenzo; Houchi, Hitoshi; Tamaki, Toshiaki; Katoh, Itsuo
CS School of Medicine, Department of Cardiovascular Surgery, The University of Tokushima, 2-50-1 Kuramoto, Tokushima, 770, Japan
SO Naunyn-Schmiedeberg's Arch. Pharmacol. (***1997***), 356(6), 756-762
CODEN: NSAPCC; ISSN: 0028-1298
PB Springer-Verlag
DT Journal
LA English
AB Several physiol. stimuli cause a rise in intracellular Ca2+ concn. ([Ca2+]i) in cardiomyocytes. This increased [Ca2+]i must be restored to physiol. resting level to ensure response to further stimuli. In the present study, the authors examd. the effect of ***neuropeptide*** ***Y*** (***NPY***), which is secreted from certain adrenergic or non-adrenergic neurons, on Ca2+ efflux from freshly isolated, quiescent adult rat cardiomyocytes. The isolated cardiomyocytes were preloaded with 45CaCl2 for 1 h. Then, the fractional release of 45Ca2+ from the cells was measured. ***NPY*** stimulated the efflux of 45Ca2+ from isolated adult rat cardiomyocytes in a concn.-dependent manner (10-8 M to 10-6 M). ***NPY*** (10-6 M)-induced Ca2+ efflux was 2.0.+-.0.16 of the total cellular content. The 45Ca2+ efflux from the cells was also stimulated by ***Y1*** receptor ***agonist*** , [Leu31, Pro34] ***NPY*** , but not by ***Y2*** receptor ***agonist*** , ***NPY13*** -36. The effect of ***NPY*** was inhibited by a peptide ***NPY*** inhibitor, ***NPY18*** -36 and a non-peptide ***NPY*** inhibitor, benextramine to a similar extent. From these results, it is conceivable that the effect of ***NPY*** on Ca2+ efflux from cardiomyocytes is mediated through ***Y1*** receptors. It was also obsd. that ***NPY*** caused a rise in [Ca2+]i to almost 150 nM. ***NPY*** -stimulated 45Ca2+ efflux was not affected by removal of extracellular Ca2+, but was dependent on the presence of extracellular Na+. Moreover, ***NPY*** caused a 22Na+ influx into the cells of about 1.6-fold over the basal value which was inhibited by amiloride and 5-(N,N-dimethyl)-amiloride, known Na+/Ca2+ exchange inhibitors. In addn., isoproterenol also caused 45Ca2+ efflux from the cells and which was enhanced by the addn. of ***NPY*** . These results suggest that ***NPY*** stimulates extracellular Na+-dependent 45Ca2+ efflux from freshly isolated adult rat cardiomyocytes, probably through its stimulatory effect on plasma membrane ***Y1*** receptors with which ***NPY*** may couple during Na+/Ca2+ exchange.

L3 ANSWER 20 OF 302 CAPLUS COPYRIGHT 2002 ACS
AN 1997:748991 CAPLUS
DN 128:30690
TI .alpha.-Helical CRF9-41 prevents anxiogenic-like effect of ***NPY*** ***Y1*** receptor ***antagonist*** BIBP3226 in rats
AU Kask, Ants; Rago, Lembit; Harro, Jaanus
CS Department of Pharmacology, University of Tartu, Tartu, EE2400, Estonia
SO NeuroReport (***1997***), 8(16), 3645-3647
CODEN: NERPEZ; ISSN: 0959-4965
PB Rapid Sci nce Publishers
DT Journal
LA English
AB We reported previously that the ***neuropeptide*** ***Y*** (***NPY***) ***Y1*** receptor ***antagonist*** , N2-(diphenylacetyl)-N-[(4-hydroxy-phenyl)methyl]-D-arginin amide

(BIBP3226) has an anxiogenic-like effect in the elevated plus maze test in rats. In this study we investigated the effect of the corticotropin-releasing factor (CRF) receptor ***antagonist*** , .alpha.-helical-CRF9-41 (.alpha.-h-CRF) on this response. BIBP3226 (5 .mu.g, i.c.v.) induced an anxiogenic-like effect, which was blocked by pretreatment with .alpha.-h-CRF at a concn. (1 .mu.g, i.c.v.) which alone failed to affect the elevated plus maze performance. Thus, the anxiogenic effect of a selective ***Y1*** receptor blocker was prevented by the blockade of CRF receptors, suggesting ***antagonistic*** effects of endogenous ***NPY*** and CRF in shaping the response to novelty.

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